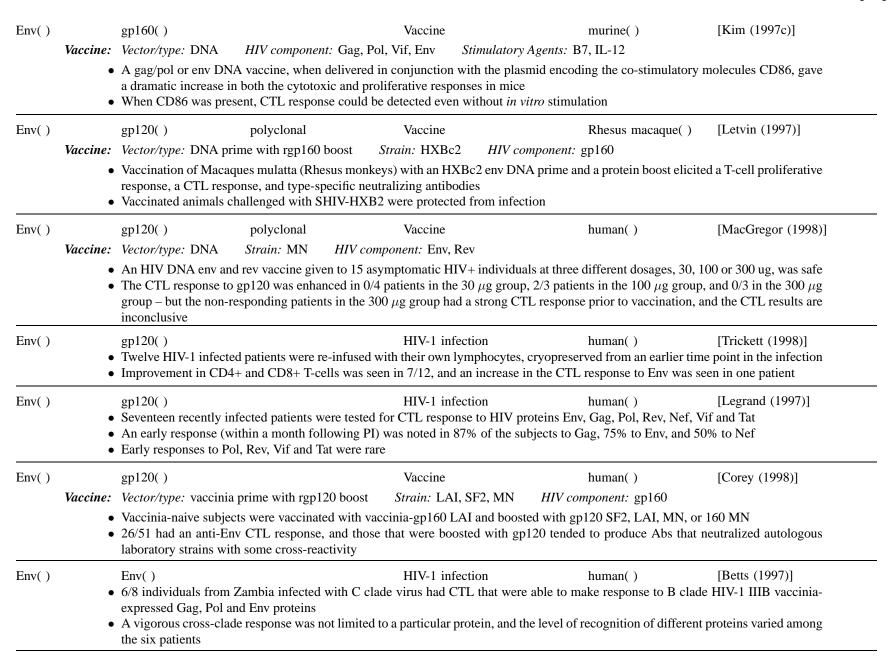
Table 19: **Env** 

	ation	<b>Author Location</b>	Sequence		Immunogen	Species(HLA)	References	
Env(306–322)		gp160()	SIRIQGPG	RAFVTIGI	Vaccine	murine(H-2D <sup>d</sup> )	[Deml (1999)]	
V	Vaccine:	Vector/type: recom cleotide, alum	binant protein	Strain: LAI	HIV component: gp160	Stimulatory Agents: Cp0	Goligodeoxynu-	
	•				alum vaccine given to BAL epitope was induced	B/c mice shifted the respon	se to Th0/Th1 from Th2,	
Env()		gp160()			Vaccine	human()	[Belshe (1998)]	
V	Vaccine:	Vector/type: canary Protease	ypox prime with	rgp120 boost	Strain: MN, LAI, SF2	HIV component: gp120	), gp41, Gag,	
	•	• The live canarypox vaccine ALVAC-HIV(vCP205) carrying MN gp120, LAI gp41, Gag and Protease, and boosted with SF-2 rpg120, was given to HIV-1 seronegative volunteers – HIV-specific Env or Gag CD8+ CTL were detected in 64% of the volunteers						
Env()		CTL response relate Chloroquine admin	ive to delivery of istration enhance	protein alone d epitope prese		human() lls (DC) with liposomes pro peptide aldehyde inhibitors	•	
					*****			
Env()	•	relative to other HI No HIV+ infants h slowly progressive	V+ infants ad no demonstral disease, and not i	ole CTL at birth	n, but Th1 responses accompassors	human() creased production of IL-2, a panied by CTL responses de ls infected with vaccinia/HI	eveloped in children with	
	•	HIV+ infants that prelative to other HI No HIV+ infants h slowly progressive CTLp frequencies gp120() Analysis of T-cell re therapy (HAART)	V+ infants ad no demonstral disease, and not in were determined ecceptor $\beta$ -chain valuecrease global C	ole CTL at birth a rapid progress by limiting dilustrated ariable region records T-cell oligonal control of the	n, but Th1 responses and decent that Th1 responses accompany to the sort that the state of the sort that the state of the	panied by CTL responses de ls infected with vaccinia/HT human() troviral therapy (ART) and h	as well as $\beta$ -chemokines, eveloped in children with V constructs  [Soudeyns (2000)]	
Env( )  Env( )	•	HIV+ infants that prelative to other HI No HIV+ infants h slowly progressive CTLp frequencies gp120() Analysis of T-cell re therapy (HAART)	V+ infants ad no demonstral disease, and not in were determined ecceptor $\beta$ -chain valuecrease global C	ole CTL at birth a rapid progress by limiting dilustrated ariable region records T-cell oligonal control of the	n, but Th1 responses accompany to the sort of the sort	panied by CTL responses de ls infected with vaccinia/HT human() troviral therapy (ART) and h	as well as $\beta$ -chemokines, eveloped in children with V constructs  [Soudeyns (2000)]	

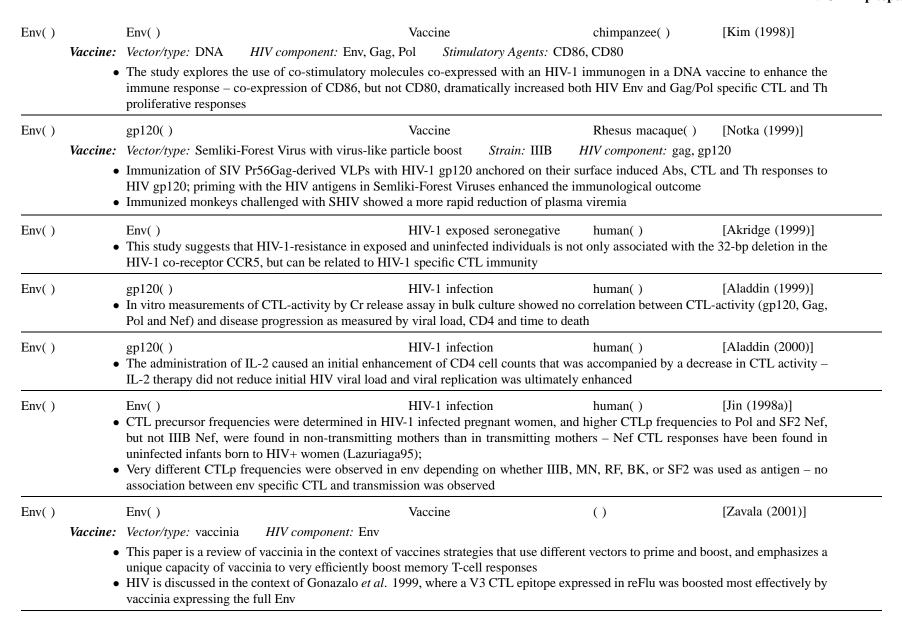
- The vaccine used was a rec canarypox with HIV-1 gp120 MN, tm/gag/protease LAI (vCP205), alone or with p24E-V3 MN synthetic peptide (CLTB-36))
- Twenty HIV negative subjects were vaccinated in phase I trial with combinations of vCP205 and CLTB-36

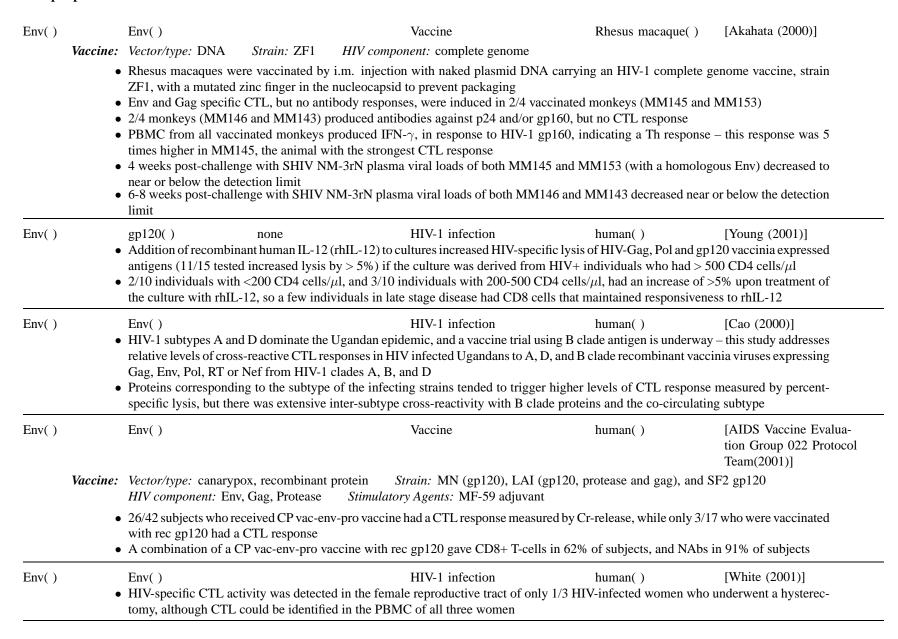
• Immunization with vCP205 induced HIV-1-specific ABs to gp160, V3, and p24 antigens, and CTL immune responses against vCP205 were detected after the fourth immunization in 33% of the subjects against Env, Gag and Pol, but the CLTB-36 peptide did not produce AB or CTL immune responses against p24 or gp160 Env() [Gamberg (1999)] Env() HIV-1 infection human() • 13/13 subjects with advanced HIV infections showed CD8 T-cell proliferation and differentiation of CTL in vitro, and six individuals showed HIV-specific responses to Gag, Pol, Env or Nef antigens • Data suggests that the functional and genetic integrity of the CD8 T-cell repertoire (TCR betaV gene intrafamily genetic diversity) remains intact through advanced HIV infection, although HIV-specific CTL activity decreases [Gorse (1999)] Env() Env() Vaccine human() Vaccine: Vector/type: canarypox prime with rgp120 boost Strain: LAI and SF2 HIV component: Env, Gag, Pro, Nef, Pro • The vaccine used was rec canarypox expressing HIV-1 env, gag, pol, nef and protease (vCP300) with or without administration of HIV-1 SF-2 rgp120 • In vitro inducible CTL activity against HIV-1 Env, Gag, Pol, and Nef antigens was observed in 79% (15/19) of vaccine recipients • The combination of vCP300 and vP1291 together resulted in an overall increase in CTL induction and detection sensitivity Env() HIV-1 infection human() [Buseyne (1998b)] • In infants with positive CTL responses, most responses showed cross-clade reactivity with somewhat diminished recognition of epitopes from different subtypes Env() gp120() Vaccine Rhesus macaque() [Shiver (1997)] Vaccine: Vector/type: DNA Strain: IIIB HIV component: gp120, gp160 • DNA vaccinations of Rhesus monkeys with a gp120 or gp160 DNA vaccine elicited a strong CD8 cytotoxic T-cell response Env() gp160() HIV-1 infection Macaca nemestrina() [Kent (1997b)] polyclonal • Macaques can be infected with HIV, and clear the infection within 6 months, so it is of interest to examine their initial immune response • A strong CTL response against env, pol and gag antigens can be detected • The CTL response peaked by 4 weeks and declined dramatically by 8 weeks • The response in the lymph nodes and peripheral blood was comparable Env() Vaccine [Kim (1997b)] gp160() murine() Vaccine: Vector/type: DNA HIV component: Gag, Pol, Vif, Env Stimulatory Agents: B7, IL-12 • A gag/pol, vif or env DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice • When IL-12 was present, CTL response could be detected even without in vitro stimulation

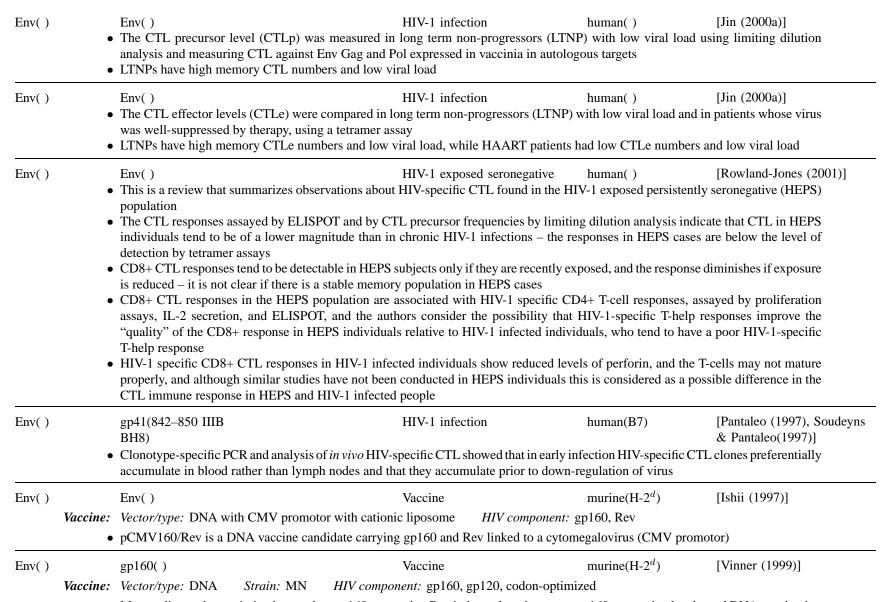


## **HIV CTL Epitopes**

Env()		Anti-NKR IgM MAb mask	HIV-1 infect natural killer cell receptor (NKR+) code this inhibitory function and increase of IL-2 from 3/5 patients, and in code	an exhibit down regulation of T-cell fased HIV-1 specific CTL activity in	phytohemagglutinin-activated				
Env()	•		HIV-1 infection between HIV Typets of Pol- and Env-specific CTL, in least	pe I plasma viral load and CTL activi					
Env()	•	Env() HIV-1 infection human() [Buseyne (1998a)]  This study showed a correlation between strong CTL memory and breadth of response in 7-12 month old infants and: remaining AIDS-free for the first year of life, higher absolute CD4 and CD8 cells, and lower viral load							
Env()		Env( ) HIV-1 exposed seronegative human( ) [Goh (1999)] 13/37 exposed uninfected individuals with repeated high-risk sexual exposure had HIV-1 specific CTL against Env, Gag, Pol, or a combination of proteins – CTL activity was correlated with a CCR5 wildtype genotype In this group, the highest CTLp frequencies were directed at Gag, but the most common response was to Env and four individuals had responses to multiple HIV-1 proteins							
Env()		Env()	Vaccine	human()	[Evans (1999)]				
	Vaccine:	Vector/type: canarypox	${\it HIV\ component:}\ gp120,gp41,Gag,$	Pro, Nef, RT					
	•	• A Canarypox vaccine expressing gp120, gp41, Gag, Protease, Nef and Pol CTL epitopes gave rise to CTL that could be detected in 61% of the volunteers – responses to Gag, Env, Nef and Pol were detected 3-6 months after the last vaccination							
Env()		Env()	Vaccine	Macaca neme	estrina( ) [Kent (1998)]				
. ,	Vaccine:	Vector/type: DNA prime wi	th vaccinia boost Strain: LAI	HIV component: Env, Gag	· · · · · · · · · · · · · · · · · · ·				
		• Priming with an HIV-DNA vaccine and boosting with a vaccinia construct induced greater levels of HIV T-cell immunity than either							
		vaccine alone  • The proliferative response to Env and Gag after the DNA vaccination had a mean SI of 1.5-4, but after boosting with rHIV-fowlpox virus, there was a 6-17 fold increase in the mean SI for HIV Gag and Env. The T help response happened despite a decrease in antibody titers, suggesting that the Th response was primarily Th1, not Th2. The CTL response was also enhanced							
Env()		Env()	Vaccine	human( )	[Salmon-Ceron (1999)]				
	Vaccine:	Vector/type: canarypox	Strain: MN, LAI HIV componer	t: gp120, gp41, Gag, Protease					
	•	<ul> <li>A live attenuated canarypox vector expressing MN gp120 and LAI gp41/gag/protease could induce CTL and a lymphoproliferative response in healthy, uninfected volunteers</li> </ul>							







Mammalian codon optimization renders gp160 expression Rev independent, increases gp160 expression levels, and DNA vaccination
of BALB/c mice yields a higher antibody response with an earlier onset than wild type

• Secreted gp120 gave higher antibody titers than membrane bound gp160 • In contrast to antibodies, synthetic codon-optimized DNA did not alter the CTL response, wild type genes generated equally strong CTL responses  $murine(H-2^d)$ [Kato (2000)] Env() () Vaccine *Vaccine: Vector/type:* peptide HIV component: V3 Stimulatory Agents: Cholera Toxin adjuvant, IL-4, GMCSF • A multicomponent peptide vaccine VC1 with cholera toxin adjuvant was given to mice. • Immunization of BALB/c mice with VC1 and CT induced a strong CTL response which was enhanced by IL-12 expressing plasmids • Immunization with VC1 and CT resulted in HIV-1 specific IgA antibody responses, which were increased by the combination of IL-4 or GM-CSF expressing plasmids gp160() Vaccine  $murine(H-2^d)$ [Kaneko (2000)] Env() Vaccine: Vector/type: DNA HIV component: gp160 Stimulatory Agents: PLG-microparticle Strain: IIIB • A PLG-microparticle encapsulated DNA encoding gp160 was given to mice. • Oral DNA vaccination of BALB/c mice induced mucosal and systemic gp160 glycoprotein-specific cellular and humoral immune responses, and mice vaccinated orally had higher resistance to HIV-env expressing vaccinia intrarectal challenge than mice vaccinated i.m. Env() Env() Vaccine  $murine(H-2^d)$ [Xin (2001)] *Vaccine: Vector/type:* adeno-associated virus (AAV) HIV component: Env, Tat, Rev Stimulatory Agents: IL-2 • An AAV vector expressing HIV-1 env, tat, and rev genes (AAV-HIV vector) was used to vaccinate BALB/c mice • A single injection stimulated and long lasting serum IgG, fecal IgA, and HIV-specific CTL • Boosting enhanced the humoral response, and IL-2 enhanced T-cell immunity Env() Env() Vaccine  $murine(H-2^d)$ [Gonzalo (1999)] Vaccine: Vector/type: influenza, vaccinia Strain: IIIB HIV component: V3, Env • The use of two different live vectors for priming and boosting has a synergistic effect on the immune response against HIV-1 – a 5-6 fold enhanced CTL response in Balb/c mice occurred when they were immunized with rec influenza virus (Flu-Env) expressing the V3 loop epitope from HIV-1 strain IIIB, and boosted with a vaccinia virus recombinant (VV-Env) expressing the complete HIV-1-IIIB env protein, comared to either immunogen alone  $murine(H-2^d)$ Env() Env() none Vaccine [McGettigan (2001)] *Vaccine: Vector/type:* rabies virus Strain: NL4-3, 89.6 HIV component: gp160 • BALB/c were immunized with a replication competent recombinant rabies virus (RV) vaccine expressing HIV-1 gp160 • A single vaccination induced induced strong and long-lasting (4.5 months) gp160-specific CTL cytotoxic responses • Although the greatest specific lysis was achieved when the vaccine strain was also used as the *in vitro* the target strain to assess the response, there was extensive CTL cross-reactivity against other B clade HIV-1 envelope proteins, implying CTL recognition of multiple epitopes within the HIV-1 envelope protein

(	כ
	ī

Env()	Env()	SIV Nef and Env CTL epitopes	SIV infection	Rhesus macaque(Mamu-	[Dzuris (2000)]			
		epitopes		A*11, -B*03, -B*	04.			
				and -B*17)	- ,			
	• Cell binding assays for Mamu molecules were employed to describe the peptide binding motifs for Mamu-A*11, -B*03, -B*03, -B*04, and -B*17 CTL epitopes – a similarity for Mamu-A*11 and -B*03 and human HLA-B*44 and -B*27, respectively, was observed – all epitopes studied were SIV epitopes, so not specifically listed here							
Env()	gp120(303–327	7)	HIV-1 infection	human(A2, A3, A B27)	11, [Ferrari (2000)]			
	<ul> <li>One of the 51 HIV-1 epitopes selected by Ferrari <i>et al.</i> as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles</li> <li>For this cluster of epitopes spanning the tip of the V3 loop, they suggest including a sequence from each clade</li> </ul>							